

What is claimed is:

1. A computer implemented method for calculating a normalization factor comprising:

providing a first intensity value ($I^{(1)}$) of a probe in a first probe array and a

5 second intensity value ($I^{(2)}$) of said probe in a second probe array;

obtaining the geometric mean (x) of said $I^{(1)}$ and said $I^{(2)}$;

calculating said normalization factor according to:

$f(x) = e^{h(x)}$, wherein said $h(x)$ is derived from referential intensities from

said first and second probe arrays.

2. The method of Claim 1 wherein said $h(x)$ is derived by relating geometric means (x_i) of first referential intensities ($RI_i^{(1)}$) in the first probe array and second referential intensities ($RI_i^{(2)}$) in the second probe array to:

$$y_i = \log \left(\frac{RI_i^{(1)}}{RI_i^{(2)}} \right).$$

3. The method of Claim 2 wherein said relating comprising:

sorting (x_i, y_i) pairs according to x_i into a plurality (m number) of bins with no overlapping;

computing medians (\bar{x}_k) of x_i 's and medians (\bar{y}_k) of y_i 's for each bin; and

interpolating said medians (\bar{x}_k, \bar{y}_k).

4. The method of Claim 3 wherein said bins are of approximately equal size.

5. The method of Claim 4 wherein said $h(x)$ is:

$$h(x) = \begin{cases} \bar{y}_1, & \text{if } x \leq \bar{x}_1 \\ w\bar{y}_1 + (1-w)\bar{y}_{i+1}, & \text{if } x \in (\bar{x}_i, \bar{x}_{i+1}), w = \frac{\bar{x}_{i+1} + 1 - x}{\bar{x}_{i+1} + 1 - \bar{x}_i}, i = 1, \dots, m-1, \\ \bar{y}_m, & \text{if } x > \bar{x}_m. \end{cases}$$

6. The method of Claim 5 wherein said m is 3.

7. A computer implemented method for comparing the expression of a gene in a first sample with a second sample comprising:

providing a first plurality of intensity values ($I_i^{(1)}$), each of which reflects the expression of said gene in said first sample, wherein said intensity values are obtained from a first nucleic acid probe array;

providing a second plurality of intensity values ($I_i^{(2)}$), each of which reflects the expression of said gene in said second sample, wherein said intensity values are obtained from a second nucleic acid probe array;

calculating a p -value using one-sided Wilcoxon's signed rank test, wherein the p -value is for a null hypothesis that $\text{median}(f(x)I_i^{(2)} - I_i^{(1)}) = 0$ and an alternative

hypothesis that $\text{median}((f(x)I_i^{(1)} - I_i^{(2)}) > 0$, wherein said $f(x)$ is a normalization factor; and

indicating whether said transcript is present based upon said p -value.

- 5 8. The method of Claim 7 further comprising a step of calculating normalization factor, said step comprising:

obtaining the geometric mean (x) of said $I_i^{(1)}$ and said $I_i^{(2)}$;

calculating said normalization factor according to:

$f(x) = e^{h(x)}$, wherein said $h(x)$ is derived from referential intensities from

10 said first and second probe arrays.

9. The method of Claim 8 wherein said $h(x)$ is derived by relating geometric means (x_i') of first referential intensities ($RI_i^{(1)}$) in said first probe array and said second referential intensities ($RI_i^{(2)}$) in said second probe array to:

$$15 \quad y_i' = \log \left(\frac{RI_i^{(1)}}{RI_i^{(2)}} \right).$$

10. The method of Claim 9 wherein said relating comprising:

sorting (x_i, y_i) pairs according to x_i into a plurality (m number) of bins with no overlapping;

20 computing medians (\bar{x}_k) of x_i 's and medians (\bar{y}_k) of y_i 's for each bin; and

interpolating said medians (\bar{x}_k, \bar{y}_k) .

11. The method of Claim 10 wherein said bins are of approximately equal size.

5 12. The method of Claim 11 wherein said $h(x)$ is:

$$h(x) = \begin{cases} \bar{y}_1, & \text{if } x \leq \bar{x}_1 \\ w\bar{y}_i + (1-w)\bar{y}_{i+1}, & \text{if } x \in (\bar{x}_i, \bar{x}_i + 1], w = \frac{\bar{x}_{i+1} - x}{\bar{x}_{i+1} - \bar{x}_i}, i = 1, \dots, m-1, \\ \bar{y}_m, & \text{if } x > \bar{x}_m. \end{cases}$$

13. The method of Claim 12 wherein said m is 3.

14. A system for calculating a normalization factor comprising:

10 a processor; and

a memory coupled with the processor, the memory storing a plurality of machine instructions that cause the processor to perform a plurality of logical steps when implemented by the processor, the logical steps comprising:

providing a first intensity value $I^{(1)}$ of a probe in a first probe array and a

15 second intensity value $I^{(2)}$ of said probe in a second probe array;

obtaining the geometric mean (x) of said $I^{(1)}$ and said $I^{(2)}$;

calculating said normalization factor according to:

$f(x) = e^{h(x)}$, wherein said $h(x)$ is derived from referential intensities from

said first and second probe arrays.

15. The system of Claim 14 wherein said $h(x)$ is derived by relating geometric means (x_i') of first referential intensities $(RI_i^{(1)})$ in the first probe array and second referential intensities $(RI_i^{(2)})$ in the second probe array to:

$$y_i = \log \left(\frac{RI_i^{(1)}}{RI_i^{(2)}} \right).$$

16. The system of Claim 15 wherein said relating comprising:
 sorting (x_i, y_i) pairs according to x_i into a plurality (m number) of bins with no overlapping;

- 10 computing medians (\bar{x}_k) of x_i 's and medians (\bar{y}_k) of y_i 's for each bin; and
 interpolating said medians (\bar{x}_k, \bar{y}_k) .

17. The system of Claim 16 wherein said bins are of approximately equal size.

- 15 18. The system of Claim 17 wherein said $h(x)$ is:

$$h(x) = \begin{cases} \bar{y}_1, & \text{if } x \leq \bar{x}_1 \\ w\bar{y}_1 + (1-w)\bar{y}_{i+1}, & \text{if } x \in (\bar{x}_i, \bar{x}_{i+1} + 1), w = \frac{\bar{x}_{i+1} + 1 - x}{\bar{x}_{i+1} + 1 - \bar{x}_i}, i = 1, \dots, m-1, \\ \bar{y}_m, & \text{if } x > \bar{x}_m. \end{cases}$$

19. The system of Claim 18 wherein said m is 3.

20. A system for comparing the expression of a gene in a first sample with a second sample comprising:

a processor; and

a memory coupled with the processor, the memory storing a plurality of machine instructions that cause the processor to perform a plurality of logical steps when implemented by the processor, the logical steps comprising:

providing a first plurality of intensity values ($I_i^{(1)}$), each of which reflects the expression of said gene in said first sample, wherein said intensity values are obtained from a first nucleic acid probe array;

providing a second plurality of intensity values ($I_i^{(2)}$), each of which reflects the expression of said gene in said second sample, wherein said intensity values are obtained from a second nucleic acid probe array;

calculating a p -value using one-sided Wilcoxon's signed rank test, wherein the p -value is for a null hypothesis that $median(f(x) I_i^{(2)} - I_i^{(1)}) = 0$ and an alternative hypothesis that $median((f(x) I_i^{(1)} - I_i^{(2)})) > 0$, wherein said $f(x)$ is a normalization factor; and

indicating whether said transcript is present based upon said p -value.

21. The system of Claim 20 further comprising a step of calculating normalization factor, said step comprising:

obtaining the geometric mean (x) of said $I_i^{(1)}$ and said $I_i^{(2)}$;

calculating said normalization factor according to:

$f(x) = e^{h(x)}$, wherein said $h(x)$ is derived from referential intensities from

said first and second probe arrays.

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22. The system of Claim 21 wherein said $h(x)$ is derived by relating geometric means (x_i') of first referential intensities ($RI_i^{(1)}$) in said first probe array and said second referential intensities ($RI_i^{(2)}$) in said second probe array to:

$$y_i' = \log \left(\frac{RI_i^{(1)}}{RI_i^{(2)}} \right).$$

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23. The system of Claim 22 wherein said relating comprising:
 sorting (x_i, y_i) pairs according to x_i into a plurality (m number) of bins with no overlapping;

computing medians (\bar{x}_k) of x_i 's and medians (\bar{y}_k) of y_i 's for each bin; and

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interpolating said medians (\bar{x}_k, \bar{y}_k).

24. The system of Claim 23 wherein said bins are of approximately equal size.

25. The system of Claim 24 wherein said $h(x)$ is:

$$h(x) = \begin{cases} \bar{y}_1, & \text{if } x \leq \bar{x}_1 \\ w\bar{y}_i + (1-w)\bar{y}_{i+1}, & \text{if } x \in (\bar{x}_i, \bar{x}_i + 1], w = \frac{\bar{x}_{i+1} - x}{\bar{x}_{i+1} - \bar{x}_i}, i = 1, \dots, m-1, \\ \bar{y}_m, & \text{if } x > \bar{x}_m. \end{cases}$$

26. The system of Claim 25 wherein said m is 3.
27. A computer software product for calculating a normalization factor comprising:
- computer program code for providing a first intensity value ($I^{(1)}$) of a probe in a first probe array and a second intensity value ($I^{(2)}$) of said probe in a second probe array;
 - computer program code for obtaining the geometric mean (x) of said $I^{(1)}$ and said $I^{(2)}$;
 - computer program code for calculating said normalization factor according to:
- $$f(x) = e^{h(x)},$$
- wherein said $h(x)$ is derived from referential intensities from said first and second probe arrays; and
- a computer readable medium for storing said codes.

28. The computer software product of Claim 27 wherein said $h(x)$ is derived by relating geometric means (x_i) of first referential intensities ($RI_i^{(1)}$) in the first probe array and second referential intensities ($RI_i^{(2)}$) in the second probe array to:

$$y_i = \log \left(\frac{RI_i^{(1)}}{RI_i^{(2)}} \right).$$

29. The computer software product of Claim 28 wherein said code for relating comprising:

computer program code for sorting (x_i, y_i) pairs according to x_i into a plurality (m number) of bins with no overlapping;

computer program code for computing medians (\bar{x}_k) of x_i 's and medians (\bar{y}_k) of y_i 's for each bin; and

computer program code for interpolating said medians (\bar{x}_k, \bar{y}_k) .

30. The computer software product of Claim 29 wherein said bins are of approximately equal size.

31. The computer software product of Claim 30 wherein said $h(x)$ is:

$$h(x) = \begin{cases} \bar{y}_1, & \text{if } x \leq \bar{x}_1 \\ w\bar{y}_1 + (1-w)\bar{y}_{i+1}, & \text{if } x \in (\bar{x}_i, \bar{x}_{i+1}), w = \frac{\bar{x}_{i+1} + 1 - x}{\bar{x}_{i+1} + 1 - \bar{x}_i}, i = 1, \dots, m-1, \\ \bar{y}_m, & \text{if } x > \bar{x}_m. \end{cases}$$

32. The computer software product of Claim 31 wherein said m is 3.

33. A computer software product for comparing the expression of a gene in a first sample with a second sample comprising:

computer program code for providing a first plurality of intensity values ($I_i^{(1)}$), each of which reflects the expression of said gene in said first sample,

wherein said intensity values are obtained from a first nucleic acid probe array;

computer program code for providing a second plurality of intensity values ($I_i^{(2)}$), each of which reflects the expression of said gene in said second sample,

wherein said intensity values are obtained from a second nucleic acid probe array;

computer program code for calculating a p -value using one-sided Wilcoxon's signed rank test, wherein the p -value is for a null hypothesis that $median(f(x) I_i^{(2)} - I_i^{(1)}) = 0$ and an alternative hypothesis that $median(f(x) I_i^{(1)} - I_i^{(2)}) > 0$, wherein said $f(x)$ is a normalization factor;

computer program code for indicating whether said transcript is present based upon said p -value; and

a computer readable medium for storing said codes.

34. The computer program code of Claim 33 further comprising computer program code for calculating normalization factor, said code comprising:

code for obtaining the geometric mean (\bar{x}) of said $I_i^{(1)}$ and said $I_i^{(2)}$;

code for calculating said normalization factor according to:

$f(x) = e^{h(x)}$, wherein said $h(x)$ is derived from referential intensities from said first and second probe arrays.

35. The computer software product of Claim 34 wherein said $h(x)$ is derived by relating geometric means (x_i') of first referential intensities ($RI_i^{(1)}$) in said first probe array and said second referential intensities ($RI_i^{(2)}$) in said second probe array to:

$$y_i' = \log \left(\frac{RI_i^{(1)}}{RI_i^{(2)}} \right).$$

36. The computer software product of Claim 35 wherein said code for relating comprising:
computer code for sorting (x_i, y_i) pairs according to x_i into a plurality (m number) of bins with no overlapping;
computer code for computing medians (\bar{x}_k) of x_i 's and medians (\bar{y}_k) of y_i 's for each bin; and
computer code for interpolating said medians (\bar{x}_k, \bar{y}_k).

37. The computer software product of Claim 36 wherein said bins are of approximately equal size.

38. The computer software product of Claim 37 wherein said $h(x)$ is:

$$h(x) = \begin{cases} \bar{y}_1, & \text{if } x \leq \bar{x}_1 \\ \bar{w}\bar{y}_i + (1-w)\bar{y}_{i+1}, & \text{if } x \in (\bar{x}_i, \bar{x}_i + 1], w = \frac{\bar{x}_{i+1} - x}{\bar{x}_{i+1} - \bar{x}_i} \\ \bar{y}_m, & \text{if } x > \bar{x}_m. \end{cases}, i = 1, \dots, m-1,$$

39. The computer software product of Claim 38 wherein said m is 3.